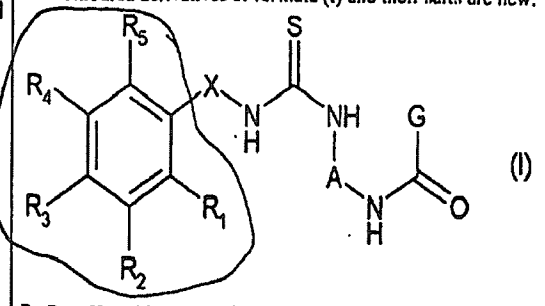
AMERICAN HOME PROD CORP *WO 200034269-A1
1998.12.09 1998-208540(+1998US-208540) *(2000.06.15)* C07D 405/12, A61K 31/33, A61P 31/12, C07D 417/12, 213/75, 213/81

Novel thiourea derivatives useful for treating diseases associated with herpes viruses (Eng)

C2000-128176 N(AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW) R(AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ TZ UG ZW)

Addnl. Data: BLOOM J D, DIGRANDI M J, DUSHIN R G, LANG S A, O'HARA B M
1999.12.06 1999WO-US28892

Thiourea derivatives of formula (I) and their salts are new.



(I)

R_1-R_5 = H, 1-6C alkyl, 2-6C alkenyl, 2-6C alkynyl, 1-6C perhaloalkyl, 3-10C cycloalkyl, 3-10C heterocycloalkyl, aryl, heteroaryl, halo, CN, NO_2, CO_2R_6, COR_6, OR_6, SR_6, SOR_6, SO_2R_6, $CONR_7R_8$, $NR_6NR_7R_8$, NR_7R_8 or W-Y-$(CH_2)_n$-Z; or
R_2+R_3 or R_3+R_4 = 3-7 membered heterocycloalkyl or heteroaryl;
R_6, R_7 = H, 1-6C alkyl, 1-6C perhaloalkyl or aryl;
R_8 = H, 1-6C alkyl, 1-6C perhaloalkyl, 3-10C cycloalkyl, 3-10C

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NOVELTY

Thiourea derivatives (I) are new.

reactant II

DETAILED DESCRIPTION

heterocycloalkyl, aryl or heteroaryl; or
R_7+R_8 = 3-7 membered heterocycloalkyl;
A = heteroaryl;
W = O, NR_6 or is absent;
Y = CO or CO_2 or is absent;
Z = 1-4C alkyl, CN, CO_2R_6, COR_6, $CONR_7R_8$, $OCOR_6$, NR_6COR_7, $OCONR_6$, OR_6, SR_6, SOR_6, SO_2R_6, $SR_6NR_7R_8$ (sic), NR_7R_8 or phenyl;
G = aryl or heteroaryl;
X = bond, NH, 1-6C alkyl, 2-6C alkenyl, 1-6C alkoxy, 1-6C thioalkyl, 1-6C alkylamino or CHJ;
J = 1-6C alkyl, 3-7C cycloalkyl, phenyl or benzyl; and
n = 1-6.

ACTIVITY

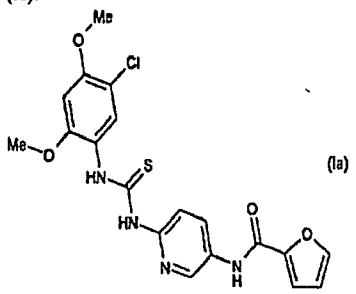
Virucide. In a V2V antiviral (ELISA) assay N-[2-(5-chloro-2,4-dimethoxy- phenyl)-thioureido]-pyridin-3-yl}-2-fluorobenzamide inhibited viral replication by 90% at a concentration of 10 micro g/ml.

USE

(I) are useful for inhibiting the replication of a herpes virus and treating herpes virus infections such as human cytomegalovirus, herpes simplex virus, and varicella zoster virus (claimed). (I) are also useful for inhibiting and/or treating diseases associated with herpes viruses including Epstein-Barr virus, human herpes viruses-6 and -7, and Kaposi herpes virus.

SPECIFIC COMPOUNDS

31 Compounds (I) are claimed e.g. furan 2-carboxylic acid {6-[3-(5-chloro-2,4-dimethoxy-phenyl)- thioureido]-pyridin-3-yl}-amide (Ia).



(Ia)

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ADMINISTRATION

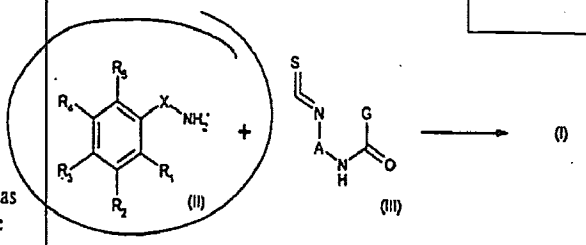
Dosage is 0.01-1000 mg/kg/day orally or 0.1-100 mg/kg/day parenterally.

EXAMPLE

To a solution of 2,5-dichloroaniline (0.16 g) in THF (20 ml) was added freshly prepared 1,1'-thiocarbonyldiimidazole (0.2 g) and the mixture was stirred for 30 minutes at room temperature. [1,2,3]-Thiadiazole-4-carboxylic acid (4-amino- phenyl) amide (0.22 g) was added and the mixture was stirred for 6 hours. Work up gave [1,2,3] thiadiazole-4-carboxylic acid {4-[3-(2,5-dichlorophenyl)-thioureido]-phenyl}-amide.

TECHNOLOGY FOCUS

Organic Chemistry - Preparation: (I) can be prepared by reacting appropriately substituted amines of formula (II) with appropriately substituted isothiocyanates of formula (III).



(II) (III) (I)

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